MEG neuroimaging of human brain development

Organizer: Blake W Johnson

Room:# 104

Date and Time: Monday, October3 / 08:30-10:30

Toward an Understanding of the Spatio-Temporal Dynamics of Human Brain Development with MEG Neuroimaging

This symposium brings together developmental MEG researchers from the US, UK, Australia, and Japan. Four of the speakers will describe their experiences using the Tristan Technologies and Yokogawa/KIT pediatric MEG systems which have recently provided new windows into brain development from infancy through the pre-school years. Two speakers will relate data from older children obtained with conventional MEG instrumentation. The talks will encompass studies of typical brain development of visual, auditory and motor processes, and studies of atypical development including fetal alcohol syndrome disorders and autism spectrum disorders. Taken together the talks of this symposium will summarize the current state of pediatric/child MEG research and illuminate future scientific and clinical directions.

Speakers:

- **Banu Ahtam** (Harvard Medical School, USA)
  "Human brain development research with MEG at Boston Children's Hospital"

  The electrophysiological aspect of brain development is studied at Boston Children's Hospital using a pediatric MEG system ("BabyMEG") (Tristan Technologies), in our new clinical MEG facility directed by Yoshio Okada. BabyMEG is a whole-head system with two layers of magnetometers: inner-layer, 270 magnetometers; and outer-layer, 35, 3-axis magnetometers; plus 9 reference magnetometers. There is an 8-9mm gap between the magnetometers and the outer surface of the helmet (sized up to 95% of boys at 36 months). The facility is equipped for studying inpatients under sedation, outpatients, and healthy children. BabyMEG is in a 2-layer MSR. Environmental noise can be rejected with noise cancellation methods (passive MSR shielding, external active shielding, signal-space projection, synthetic gradiometer). Spontaneous brain activity can be monitored in real-time (collaboration with MGH MEG Team, directed by Matti Hämäläinen). We use a closed-cycle helium recycler (Cryomech). We can perform simultaneous MEG/EEG measurements. We study epileptiform activity and localization of focal generators, and in healthy children, sleep, detailed characterization of sensory and motor areas of the cortex, and language development. We will expand our studies to other disorders such as cerebral palsy. The features of our facility expand the versatility and power of MEG for studying human brain development.

- **J Christopher Edgar** (Children's Hospital of Philadelphia, USA)
  "The maturation of auditory responses in infants and young children: a cross-sectional study from 6 to 59 months"

  An understanding of the maturation of auditory cortex responses in typically developing infants and toddlers is needed to identify auditory processing abnormalities in infants at risk for neurodevelopmental disorders. The availability of infant and young child magnetoencephalography (MEG) systems may now provide near optimal assessment of left and right hemisphere auditory neuromagnetic responses in young populations. To assess the performance of a novel whole-head infant MEG system, a cross-sectional study examined the maturation of left and right auditory cortex responses in children 6- to 59-months of age. Blocks of 1000Hz (1st and 3rd blocks) and 500Hz tones (2nd block) were presented while MEG data were recorded using an infant/young child biomagnetometer (Artemis123). Data were

obtained from 29 children (11 males; 6- to 59-months). Latency measures were obtained for the first positive-to-negative evoked response waveform complex in each hemisphere. Findings of strong age and latency associations, sensitivity to tone frequency, and good test-retest reliability support the viability of longitudinal infant MEG studies that include younger participants as well as studies examining auditory processing abnormalities in infants at risk for neurodevelopmental disorders. Building upon the above, preliminary data from a longitudinal study examining brain structure-function associations in infants (3-to-18 months) are presented.

- **Mitsuru Kikuchi** (Kanazawa Univ., Japan)
"Atypical development of the auditory system in children with autism spectrum disorder"

Brain responses to auditory stimuli in children with autism spectrum disorder (ASD) have been studied as a physiological indicator of language acquisition, cerebral laterality and regional connectivity. The earliest cortical component of the auditory evoked field (AEF) (i.e., the P1m) is a prominent component in 1- to 10-year-old children. Recently, a child-customized MEG device has facilitated the acquisition of bi-hemispheric recordings, even in young children. Using the child-customized MEG device, we reported that the children with ASD exhibited significantly less leftward lateralization in their P1m intensity compared with the typically developing (TD) children (2 to 5 years old). In addition, we reported that language-related performance was reflected in the dipole intensity of the P1m in TD young children (2 to 5 years old) even after controlling for confounding factors (e.g., age). Our recent study with wider age range group (3 to 10 years old) demonstrated an inverted U-shaped growth curve for the P1m dipole intensity in the left hemisphere in TD children, whereas more diversified age-related distribution was observed in children with ASD. These our results from MEG studies contribute to our understanding of diversified pathophysiological mechanisms in the central nervous systems in young children with ASD.

- **Wei He** (Macquarie Univ., Australia)
"Effective connectivity of core brain networks for perception and cognition in preschool age children"

Theoretical frameworks for understanding functional brain maturation suggest an increasingly fine-grained brain network including progressively specialized regional activity and more organized patterns of inter-regional connectivity during development. However, due to the practical challenges of conducting brain-imaging studies with preschool children, there is little direct evidence bearing on the development of such connections in the human brain. We measured brain activity in preschool age children with a custom-sized paediatric MEG system and examined connectivity patterns with dynamic causal modelling (DCM). Face responses (M170 and M250) were obtained in 10 children (63.6 ± 9.96 months) and auditory mismatch (MMF) fields were obtained from 25 children (51.83 ± 7.77 months). DCM results showed a forward regulation modulated by face repetitions within the immature face network that does not exist in adults, and for MMF, an extra frontal lobe connection to auditory cortex. These results are the first MEG evidence that bear directly on competing theories of human brain development in core brain networks during the preschool years.

- **Klaus Kessler** (Aston Univ., UK)
"Local dysregulation, global hypoconnectivity, and deficient predictive coding in ASC"

Gamma band activity (GBA) has been investigated as a proxy measure for local connectivity in order to test the hypothesis that connectivity at the local scale could be overexpressed in autism spectrum conditions (ASC), resulting in symptoms such as hypersensitivity to sensory stimulation (“the world is too intense”). However, mixed results have shown both elevated and reduced GBA in ASC. Furthermore, physiological and electrophysiological measures on ASC show that inhibitory neuron density is reduced and local cross-frequency coupling is under-expressed, suggesting that local dysregulation in form of a suboptimal balance between excitation and inhibition could provide a more plausible alternative

explanation for the apparently paradoxical coexistence of enhanced and reduced GBA and of hyper- and hyposensitivities in ASC. In conjunction with consistently reported reductions in long-range connectivity in ASC, an overall picture of local disorganisation including deficient top-down input from control areas of the brain emerges that is compatible with the notion that predictive coding might be particularly affected in ASC. In the light of these theoretical considerations we will present preliminary MEG data and analysis focussing on GBA and cross-frequency coupling.

- **Julia M. Stephen** (The Mind Research Network, USA)
"Visual deficits in children with fetal alcohol spectrum disorder – implications for understanding normal development"

  Fetal alcohol spectrum disorder (FASD) is a neurodevelopmental disorder that is defined by both structural and functional impairments associated with prenatal alcohol exposure. Initial studies implicated executive function deficits even in the absence of facial dysmorphias associated with fetal alcohol syndrome. Our recent MEG studies in adolescents (aged 12-21 years) indicate that both basic visual processing and cognitive functioning are impaired in children with FASD. Using a prosaccade task we have identified delays in visual processing in children with FASD relative to age-matched controls. Development of frontal networks was investigated using an antisaccade task with differences in the eye gaze network in children with FASD relative to healthy controls. Furthermore, our more recent studies in younger children with FASD (8-12 years) indicate that these processing delays are observed during performance of a visual go-nogo task, while additional deficits are observed in frontal cortex. Finally, our most recent results indicate that MEG differentiates children with FASD from children with attention deficit hyperactivity disorder (ADHD), despite the challenges of differentiating these groups based on neuropsychological testing. These results provide additional evidence that measurement of visual processing networks using MEG may be an important tool for early identification and classification of neurodevelopmental disorders.